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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/689,149	10/20/2003	Miri Seiberg	3282-P02872US04	6375

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DANN, DORFMAN, HERRELL & SKILLMAN
1601 MARKET STREET
SUITE 2400
PHILADELPHIA, PA 19103-2307

EXAMINER	
PACKARD, BENJAMIN J	

ART UNIT	PAPER NUMBER
1612	

MAIL DATE	DELIVERY MODE
12/07/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/689,149	SEIBERG ET AL.	
	Examiner	Art Unit	
	BENJAMIN PACKARD	1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 September 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-32* is/are pending in the application.

4a) Of the above claim(s) *5-8,10-12,14-16,21-24,26-28 and 30-32* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,9,13,17-20,25 and 29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 09/29/10 has been entered.

Applicants' arguments, filed 09/29/10, have been fully considered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1-4, 9, 13, 17-20, 25, and 29 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Ryan (US 4,906,457, see IDS filed 07/12/04) in view of Maeda et al (JP 07010772, see IDS filed 07/12/04).

Applicants again assert BBI is unique from Kunitz-type soybean trypsin inhibitors and BBI, both a chymotrypsin and trypsin inhibitor, is the only soybean product exemplified by the '457 patent. Similarly, Applicants assert the '457 patent does not

teach or suggest the use of a trypsin specific inhibitor for reducing the risk of skin cancer.

Applicants also note references including Hennedy (Amer J Clin Ntr (998) 68:14065-1412S) and some of its cited references which disclose ten years after the '457 patent was filed that the skilled artisan thought the ability to inhibit carcinogenesis is associated with the activity to inhibit chymotrypsin. For instance, Yavelow et al (Proc Natl Acad Sci (1985) 82:5395-5399) indicates the chymotrypsin-inhibitory activity of the BBI is essential to suppress radiation-induced transformation *in vitro*. Applicants now cite Kennedy (Pharmacol Ther (1998) 78:167-209) which teaches BBIC does not include Kunitz-type soybean trypsin inhibitors and that TI may be removed from soy bean extract and still have activity.

Applicants also note the secondary reference only teaches Kunitz-type soybean trypsin inhibitors for the suppression of inflammatory edema, not to reduce the risk of cutaneous tumor development.

Finally, Applicants assert the evidence presented shows unexpected results where administration is via a liposomal delivery system.

Examiner disagrees. First, Examiner notes 35 U.S.C. § 282 (2000) recites "A patent shall be presumed valid. Each claim of a patent (whether in independent, dependent, or multiple dependent form) shall be presumed valid independently of the validity of other claims; dependent or multiple dependent claims shall be presumed valid even though dependent upon an invalid claim." As such,, the '457 specifically claims "A method for treating skin to reduce the risk of skin cancer included by sunlight or

ultraviolet radiation, comprising applying an effective amount of at least one protease enzyme inhibiting agent ,,," (claim 13) and "..wherein said effective amount of at least one protease enzyme inhibiting agent is selected from the group consisting of ... protease enzyme inhibitors of the trypsin class of protease, ... protease enzyme inhibitors of the Bowman Birk inhibitor family..." (claim 17). Note, the Markush group of claim 17 specifically delineates both inhibitors of the BBI family, and as a separate group, protease enzyme inhibitors of the trypsin class of protease. Therefore, the '457 explicitly teaches the use of protease enzyme inhibitors of the trypsin class of protease, as well as inhibitors of the BBI family. As claimed, the method is presumed enabled and the skilled artisan would have a reasonable expectation that practicing the method would provide the desired effect. While the working embodiments focus on the BBI family inhibitors, the working and preferred embodiments do not limit the claimed invention, but instead the claims themselves delineate the patented invention. Thus, Applicants assertion that there is no teaching of using trypsin class of protease inhibitors appears to be an invalid assertion. Thus, cited teachings of ideas with regards to BBI and opinions of BBI activity are not sufficient to overcome the presumption of enablement afforded the patentee of the '457 patent.

Second, the references submitted by Applicant do in fact suggest BBIs were the preferred protease inhibitors at the time of filing and thought by some to provide the skin protective properties, but such teaching does not negate the fact that protease enzyme inhibitors of the trypsin class of protease were explicitly disclosed, claimed, and patented as useful inhibitors in the same method as instantly claimed. Examiner also

disagrees that Kennedy teaches away where there is disclosure that the BBI containing preparation is used rather than use of whole soybeans due to the TI activity which can have side effects in mouse models. Specifically, the reference teaches the reduction of TI activity in order to increase the activity of BBIC, but does not assert TI does not have beneficial properties, only that BBIC appears to be the preferred family of protease inhibitors and therefore are isolated to increase their concentration. Further, where the composition is administered topically, as claimed in the primary reference, it is unclear whether the potential pancreatic toxic effect will occur or whether that result is limited to oral administration.

Third, the secondary reference is cited not for the method disclosed therein, but for the teaching that soybean Kunitz-type trypsin inhibitors were known in the art and when practicing the method of the primary reference, the skilled artisan would select known trypsin inhibitors.

Finally, Examiner disagrees that the results show an unexpected improvement. First, applying Applicants suggestion that the proper comparison should be between the administration of STI in liposomes to administration of only liposomes, Examiner notes there is a substantial increase in tumor volume when comparing no treatment with liposomal only treatment. Therefore it is unclear why a liposomal dosage is administered, given there would be expected to be an increase in tumor volume size per se. Even assuming the skilled artisan might still use liposomes, Examiner notes the results show the increase in tumor volume caused by the liposomes is simply countered

by the effect of STI, producing a net change which is not statistically different than no treatment at all.

Additionally, Applicants assertion that non-denatured shows an improved effect is not found persuasive either, given there is no evidence that denatured STI would be considered a trypsin inhibitor. To the contrary, the skilled artisan would reasonably expect a decrease in activity due to the denaturing of the proteins. As such, the method claimed in the primary reference would be negated and there would be no reason to administer the deactivated proteins, given the purpose is to administer protease inhibitors which have trypsin inhibitory activity.

Conclusion

No claims allowed.

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BENJAMIN PACKARD whose telephone number is (571)270-3440. The examiner can normally be reached on M-R 8-5 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick Krass can be reached on 571-272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Benjamin Packard/
Examiner, Art Unit 1612

/Frederick Krass/

Supervisory Patent Examiner, Art Unit 1612